Evidence-based Approaches to Deciphering Acute versus Chronic Wound Infections:

Microbiology, Immunology, Clinical and Therapeutic Insights. *

The Problem:

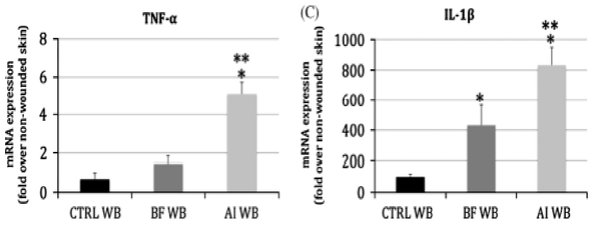
Wound infection and chronic, hard-to-heal wounds represent significant challenges in healthcare, marked by a complex interplay between microbial pathogens, antimicrobial therapy, and the host's immune response. This is further challenged by the compromised immune health associated with our aging population as well as increasing chronic disease prevalence. One emerging factor contributing to the persistence of infection and wound chronicity is the formation of biofilms. Biofilms, composed of communities of bacteria and fungi encased in a protective extracellular matrix, exhibit enhanced tolerance to conventional antibiotics and antiseptics. This resilience not only complicates wound infection management but also underscores the urgent need to revise understanding as well as therapeutic approaches. Without these revisions the rampant and indiscriminate use of antibiotics will continue to exacerbate our current global problem of antibiotic resistance, further diminishing the effectiveness of these critical drugs as well as intensify the complications associated with wound chronicity.

Method:

Narrative review of current literature on acute and chronic infections in wounds, biofilm tolerance, antibiotic use in wounds, antimicrobial stewardship

What was discovered?

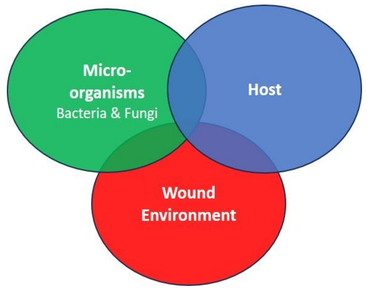
A narrative literature review revealed that there is objective, *in vivo* research confirming the existence of **two types of wound infection, acute and chronic**; the latter relating to the tolerance of the **biofilm phenotype**. These different types of wound infection have unique clinical characteristics involving overt and covert clinical signs and they require distinctive treatment strategies



In this *in vivo*, full thickness wound model, biofilm infection elicited a significantly lower-grade host inflammatory response ($p < 0.05$), than acutely infected wounds, indicating a true phenotypic difference in the bacteria–host response between **these two types of infection**

Gurjala AN, Geringer MR, Seth AK, et al. Development of a novel, highly quantitative in vivo model for the study of biofilm-impaired cutaneous wound healing. Wound Repair Regen. 2011 May-Jun; 19(3):400-10. doi: 10.1111/j.1524-475X.2011.00690.x

Infection RISK is multifactorial



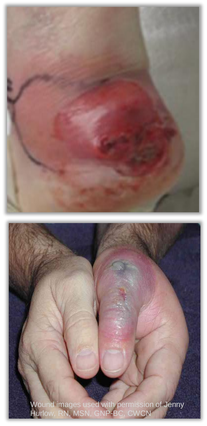
Infection risk involves:

1. The strength of the host e.g. comorbidities, nutrition, hygiene
2. Wound environment e.g. necrotic tissue, inadequate topical dressing management
3. Microorganisms e.g. virulence, quantity, phenotype (biofilm/planktonic)

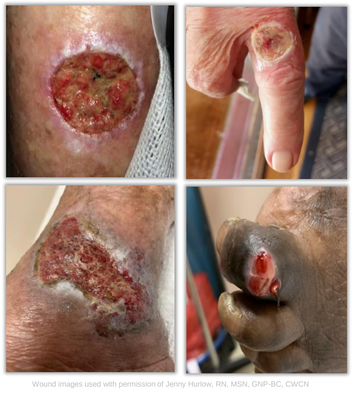
Wound Infection:
A host inflammatory response to interfering microorganisms that either directly or indirectly damage viable host tissue, hence preventing wound healing.

Acute infections in wounds: Involves invasion of viable wound tissue by metabolically active **planktonic** microorganisms that trigger a host inflammatory response. This inflammatory response is **overt** and triggers the classic signs and symptom of infection; calor, dolor, rubor, tumor.
An acute infection is a **host-controlled** inflammatory response because the innate immune system is equipped to defend against invasion of planktonic bacteria.

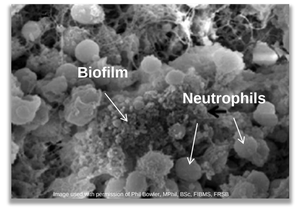
This defensive response can be aided by the use of **appropriately chosen systemic antibiotic** therapy.



Chronic infections in wounds: Manifests as an unclear and prolonged **covert** inflammatory condition in which a parasitic **biofilm** is the root of the problem.
Clinical signs of a chronic wound infection are a frustrated, low grade inflammation resulting in delayed healing, excessive exudate, dull, dark red, friable, and pocketing of granulation tissue, foul odor, pain, and absence of acute infection.
A chronic infection is a **microbe controlled** inflammatory response because biofilm is the root of the problem. The immune response is not equipped to managed a persistent biofilm that is, by nature, also **tolerant to both topical and systemic antimicrobials.**



In **chronic infections**, a vicious cycle exists whereby sustained inflammation caused by persistent biofilm leads to excessive and ineffective production of neutrophils. In turn, this leads to production of neutrophil extracellular traps (NETS) which results in tissue damage and amplifies biofilm formation. Neutrophils cannot attack bacteria within biofilm which leads to 'frustrated' neutrophil function and host tissue damage.



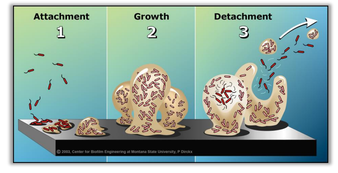
Wolcott described this as 'Biofilm-hijacked' inflammation

Treatment for a chronically infected wound requires early and routine use of Wound Hygiene techniques designed to control biofilm on the wound bed. This involves:

1. Cleansing the wound with a noncytotoxic antiseptic wound cleanser
2. Debridement of unwanted tissues (slough, devitalized tissue, etc.) using sharp, mechanical, surgical, or ultrasonic techniques. Autolytic debridement is not adequate.
3. Re-cleansing the wound to include attention to periulcer skin and refashioning of edges to open and facilitate epithelial migration
4. Treat with a topical antiseptic dressing shown to inhibit biofilm re-formation.

Systemic antibiotics are not indicated for a chronically infected wound.

A **chronic infection can become an acute infection** in an at-risk patient. Planktonic microorganisms dispersing from a mature biofilm in a chronically infected wound can lead to an acute infection.
A**ppropriately chosen systemic antibiotics** can be beneficial for management of acute wound infection.



Discussion:

A chronic, hard-to-heal wound involves a chronic, biofilm related infection. An improved understanding of the distinctive characteristics of the two types of wound infection and how these relate to wound treatment and chronicity will promote more focused, effective wound management and help to limit ineffective use of antibiotics therefore helping to control our growing global problem related to antibiotic resistance.

* Reference: Hurlow J, Bowler PG. Acute and chronic wound infections: microbiological, immunological, clinical and therapeutic distinctions. J Wound Care. 2022 May 2;31(5):436-445. doi: 10.12968/jowc.2022.31.5.436. PMID: 35579319